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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/006,177	12/04/2001	Venky Ramakrishna	26747-35	2918

7590 01/11/2005

Alan J. Grant, Esq.
c/o Carella, Byrne, Bain, Gilfillan,
Cecchi, Stewart & Olstein
6 Becker Farm Road
Roseland, NJ 07068

EXAMINER

YU, MISOOK

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 01/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/006,177

Applicant(s)

RAMAKRISHNA ET AL.

Examiner

MISOOK YU, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 October 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) 9-14 and 16-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8 and 15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>06/13/03</u> . | 6) <input checked="" type="checkbox"/> Other: <u>See Continuation Sheet</u> . |

Continuation of Attachment(s) 6). Other: Exhibits A, and B (sequence alignments).

DETAILED ACTION

Election/Restrictions

Applicant's election of group 4 drawn to immunogen comprising SEQ ID NO:4 in the reply filed on 10/25/2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 9-14, and 16-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claim 9 was included in the immunogen products groups 1-20. However, group 9 is limited to Mage D protein, which comprises SEQ ID NO:17 according to the specification at page 19. Therefore claim 9 is drawn to non-elected invention.

Claims 1-28 are pending. Claims 1-8, and 15 are examined on merits to the extent the claims read on SEQ ID NO:4.

Claim Objections

Claims 1-8, and 15 are objected to because of the following informalities: the claims have not been amended to reflect the election. The claims are still drawn to multiple inventions. Appropriate correction is required.

Claims 5-8 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 5-8

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depend on claim 1. Every species in dependent claims should belong to the property boundary set by the independent claim 1. Claim 1 is drawn to genus of polypeptides comprising SEQ ID NO:4 (the elected invention). Therefore, any species that does not comprise SEQ ID NO:4 is outside of the property boundary of the independent claim 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7, and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The scope encompassed by claim 7 is confusing and vague. The specification at paragraph [0078] discloses "Conservative substitutions are herein defined as exchanges within one of the following five groups: Group 1--small aliphatic, nonpolar or slightly polar residues (Ala, Ser, Thr, Pro, Gly); Group 2--polar, negatively charged residues and their amides (Asp, Asn, Glu, Gln); Group 3--polar, positively charged residues (His, Arg, Lys); Group 4--large, aliphatic, nonpolar residues (Met, Leu, lie, Val, Cys); and Group 4--large, aromatic residues (Phe, Tyr, Trp)." The specification does not define "hydrophobic amino acid". Voet et al., (Biochemistry, John Wiley & Sons, 1990, pages 60-63 only) at page 63, left column teach that "the most useful way of classifying the 20 standard amino acids is according to the polarities of their side chains (R groups). This is because proteins fold to their native conformations largely in

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response to the tendency to remove their hydrophobic side chains from contact with water and to solvate their hydrophilic side chains.” This disclosure suggests that the nine amino acids at page 60, Table 4-1 under the heading “amino acids with nonpolar side chains” are nonpolar (i.e. hydrophobic) amino acids. However, the instant specification at paragraph [0078] classifies hydrophilic amino acids such as Ser with the hydrophilic Ala as the conservative substitution. It is not clear whether Ala to Ser substitution is within the property boundary of claim 7 given the specification does not define “hydrophobic amino acid”. It appears that Ala to Ser substitution is not the substitution of one hydrophobic amino acid unit by another hydrophobic amino acid according to the definition of polarities of amino acids as disclosed in Voet et al. Further, it appears that Phe to Leu change is the substitution of one hydrophobic amino acid unit by another hydrophobic amino acid according to the definition of polarities of amino acids as disclosed in Voet et al. Given claim 7 depends on claim 6, drawn to a conservative hydrophobic amino acid substitution, none of the four groups contains only hydrophobic amino acids defined by Voet et al., (note this is a textbook published more than a decade ago). Thus, the property boundary set by instant claim 7 is vague. For the purpose of this Office action, the Office will assume any amino acid of those 9 amino acids having nonpolar R groups at page 60 of Voet et al., meets the limitation of “hydrophobic amino acid” in claim 7 (see art rejection below). However, this treatment does not relieve applicant the burden of responding to this rejection.

Claim 8 recites the limitation "said oligopeptide" in line 2. There is insufficient antecedent basis for this limitation in the claim.

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8, and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The applicable standard for the written description requirement can be found: MPEP 2163; University of California v. Eli Lilly, 43 USPQ2d 1398 at 1407; PTO Written Description Guidelines; Enzo Biochem Inc. v. Gen-Prove Inc., 63 USPQ2d 1609; Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111; and University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC 2004).

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

In this case, the only factor present in the base claim 1 is a partial structure i.e. SEQ ID NO:4 to describe the claimed genus of polypeptides. Claim 1 as currently construed encompasses full-length proteins such as differently spliced isoforms that are

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not further described because the claim as constructed with the open transitional phrase “comprising” in respect to the claimed isolated polypeptide. There is substantial variability among the species encompassed within the scope of the claims because SEQ ID NO:4 is only a fragment of any full-length protein. They are structurally unrelated. A description of a genus of protein may be achieved by means of a recitation of a representative number of proteins comprising the recited sequence, i.e. SEQ ID NO:4 defined by amino acid sequences, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. The breath of the claims as reading on proteins encoded by differently spliced isoforms of a gene, or homologs from different species yet to be discovered. There is lack of correlation between the structure and the function of the genes comprising the partial sequence, i.e. SEQ ID NO:4, therefore, it is concluded that the written description requirement is not satisfied.

Claims 2-4 depend on claim 1, drawn to an isolated polypeptide whose amino acid sequence comprises at least one epitopic peptide from the 20 different Markush groups as the alternative choice. Claims 2-4 describe the single polypeptide of the base claim 1 as having at least 2-4 epitopic peptides. Neither the specification nor any art of record describes any isolated polypeptide with either repeat(s) of up to four of SEQ ID NO:4 within the polypeptide or SEQ ID NO:4 or any other epitopic peptide sequence described in the base claim 1.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought,

he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, given that the specification has only described the art-known topoisomerase II comprising the instant SEQ ID NO:4 (see page 17 lines 4-10 of the instant specification). Therefore, only the art-known topoisomerase II polypeptide comprising instant SEQ ID NO:4, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

Claim 15 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibody production in a heterologous host, does not reasonably provide enablement for use as vaccine for treatment of cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is ☐undue☐ include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and

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8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

This rejection is made because the specification fails to teach how to use the claimed polypeptides as a vaccine for **inducing an anti-tumor T-cell immune response** without undue experimentation.

The specification teaches at pages 50-51 that SEQ ID NO:4 binds to HLA-A2. Based on this discovery, the specification asserts that a polypeptide comprising SEQ ID NO:4 could be use as vaccine for generating anti- tumor immunity (note the title of the application). However, the specification fails to demonstrate the efficacy of the vaccine comprising polypeptide comprising SEQ ID NO:4 on the induction of ant-tumor response, which reduces tumor burden or prevent the formation of a tumor in a patient. Searching potential T-cell epitopes in any protein using existing software (this use is considered as research, not patentable use) does not require undue experimentation; the asserted actual patentable use is to use the claimed polypeptide as vaccine for treating or preventing cancer. Undue experimentation is required to use the claimed vaccine to elicit anti-tumor response in a subject because the current state of art teaches that cancer therapy using a vaccine comprising a polypeptide is unpredictable. The specification fails to teach how administration of the claimed polypeptide would produce a sufficient amount of CTLs, NK cells and/or any other T cells to kill tumors in an animal or human that has malignant cells expressing a polypeptide comprising instant SEQ ID NO:4. Adachi et al., (cited below, see the art rejection) teach the polypeptide comprising instant SEQ ID NO:4 is a self antigen, rather than a mutated

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antigen, as it is expressed on normal tissues, and that self-tolerance may eliminate T cells that are capable of recognizing these epitopes with high avidity (Sherman, LA et al, 1998, Critical reviews in Immunol, 18(1-2): 47-54, see especially at the abstract and Table 2). In other words, only CTLs with low affinity are left, which may not be optimal for tumor elimination *in vivo*. One of the problem is that after some period of time in the presence of tumor cells, T cells may lose their functional activity. Lauritzsen et al (International Journal of Cancer, 1998, Vol. 78, pp. 216-222) teach that clonal deletions of thymocytes is a major event in T-cell tolerance which could lead to a tumor escape mechanism. In transgenic mice homozygous for HLA-specific CD+4 T-cells which are specific for a MOPC315 plasmacytoma, injection of a large number of tumor cells results in apoptosis of immature and mature transgenic CD+4+8 and CD+4 thymocytes. This negative selection was specific for the transgenic thymocytes that would complement the idiotype of the immunoglobulins of the MOPC315 plasmacytoma, because injection of tumor cells from a plasmacytoma which had a different idiotype of immunoglobulins failed to elicit the clonal deletion. Lauritzsen et al teach that injection of purified MOPC315 protein, versus the tumor cells, caused a profound reduction of the specific thymocytes specific to the idiotype of the plasmacytoma. Lauritzsen et al conclude that deletion of tumor specific thymocytes may represent a major escape mechanism in patients with cancers that secrete or shed antigens. In the instant case, the polypeptide comprising SEQ ID NO:4 is a known self-antigen. It would be reasonable to conclude that said normal antigens are presented within the thymus to developing thymocytes and T-cells with high affinity for said antigens are deleted as

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"self". It would be also reasonable to conclude that administration of the claimed polypeptides or cells expressing said polypeptides would not result in an efficacious vaccine as a T-cell response would not be evoked due to the process of clonal deletion in the thymus, rendering the host devoid of T-cells which are specific to the self-protein. Sarma et al (Journal of Experimental Medicine, 1999, Vol. 189, pp. 811-820) states that a critical issue in therapeutic regiments comprising the administration of tumor antigens for immunotherapy is whether unmutated tumor antigens which are expressed in normal cells impose special restrictions on the CTL response in vivo. Using transgenic mice wherein the antigen specific T cells specific for the P1A non-mutated tumor antigen are expressed at high levels and remain responsive to the P1A antigen when assayed in vitro, it was found that P1A antigen expressed in the thymus resulted in clonal deletion of said specific T-cells. Sarma et al note that although said transgenic mice produce an overwhelming majority of T cells that are specific for P1A, said mice are no more resistant to cells expressing P1A than non-transgenic litter mates. Sarma et al concludes that even though P1A can be a tumor rejection antigen, the effector function of P1A specific CTL is restrained in vivo and that these results have important implications for the strategy of tumor immunotherapy. With regard to the isolation of two T-cells which are specific for the instant antigen presented in the context of HLA-A24, it cannot be determined if this is a reliable indicator that in all patients, with any of the types of cancers listed on page 20, would have a T-cell available after thymic selection which would react with said antigen in the context of HLA-A24 or any other MHC molecule.

The specification does not provided any evidence that a polypeptide comprising instant SEQ ID NO:4 might be able to be used for cancer therapy or prevention. It is concluded based on the references discussed above, that the state of the art with respect to treating cancer patients of administering tumor antigens is unpredictable. The specification does not provide any disclosure that the administration of the claimed polypeptides would generate CTLs which lyse the cells of a tumor. Considering the limited guidance, no working examples in the specification, and the unpredictability in the art, it is concluded that undue experimentation is required to use the claimed polypeptide for vaccine in prevention or treating cancer.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Adachi et al., (1992, Nucleic Acids Research, vol. 20, pages 5297-5303).

Claims 1, and 15 are interpreted as drawn to immunogen (claim 1), or vaccine (claim 15) comprising an isolated polypeptide comprising SEQ ID NO:4 as the active ingredient for intended use as immunogen or vaccine, wherein claim 15 further specifies the active ingredient is in a pharmaceutically acceptable carrier.

Adachi et al., teach the mouse topoisomerase II protein sequence comprising instant SEQ ID NO:4 (note Exhibit A, the sequence alignment showing that instant SEQ

ID NO:4 matches 100% to amino acid #827 to 835 of the mouse topoisomerase II protein) at Fig. 1, an isolated polypeptide in Fig. 4, also teach vaccine in a pharmaceutically acceptable carrier (see at page 20, left column).

Claims 5, 7, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by US Pat. 5,645,994 (Jul. 8, 1997).

Claims 5, 7, and 8 are interpreted as drawn to immunogen comprising an polypeptide whose amino acid sequence comprises an epitope that differs from SEQ ID NO:4, wherein the difference is not more than one amino acid (claim 5), wherein the difference is the substitution of one hydrophobic amino acid unit by another hydrophobic amino acid (claim 7), and wherein difference is the addition or deletion of one amino acid.

US Pat. 5,645,994 at columns 43-46 teaches SEQ ID NO:30 polypeptide whose amino acid sequence comprises an epitope that differs from SEQ ID NO:4, wherein the difference is one amino acid, i.e. at position #1 of the instant SEQ ID NO:4, wherein the difference is the substitution of one hydrophobic amino acid unit by another hydrophobic amino acid (i.e. Phe of instant SEQ ID NO:4 to Leu of the art, Note the attached Exhibit B). As for claim 8, SEQ ID NO:30 of US Pat. 5,645,994, which lack the first amino acid from instant SEQ ID NO:4 meets the limitation "deletion of one amino acid". The preamble recitation of "immunogen" is merely suggestive of an intended use and is not given patentable weight for purposes of comparing the claims with the prior art. The claims read on the an isolated polypeptide *per se*.

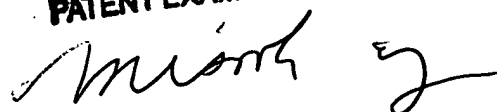
Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey C Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MISOOK YU, Ph.D.
Examiner
Art Unit 1642

MISOOK YU
PATENT EXAMINER


QY 1 FLYDDNQRV 9
|||||
DB 91 FLYDDNQRV 99

RESULT 3

JN0598
DNA topoisomerase (ATP-hydrolyzing) (EC 5.99.1.3) - rat
N;Alternate names: DNA topoisomerase II
C;Species: Rattus norvegicus (Norway rat)
C;Date: 03-Feb-1994 #sequence_revision 03-Feb-1994 #text_change 16-Jul-1999
C;Accession: JN0598; S32012
R;Park, S.H.; Yoon, J.H.; Kwon, Y.D.; Park, S.D.
Biochem. Biophys. Res. Commun. 193, 787-793, 1993
A;Title: Nucleotide sequence analysis of the cDNA for rat DNA topoisomerase II.
A;Reference number: JN0598; MUID:93290677; PMID:8390253
A;Accession: JN0598
A;Status: nucleic acid sequence not shown
A;Molecule type: DNA
A;Residues: 1-1526 <PAR>
A;Cross-references: EMBL:Z19552; NID:G57963; PIDN:CAA79611.1; PID:G57964
A;Experimental source: testis
A;Note: the authors translated the codon GTG for residue 3 as Leu
C;Comment: This enzyme is required for the segregation of circular DNA molecules after
C;Genetics: rTOP2
C;Superfamily: eukaryotic type II DNA topoisomerase; phase T4 DNA topoisomerase (ATP-hy
C;Keywords: ATP; DNA recombination; DNA repair; DNA replication; isomerase
F;589-916/Domain: phase T4 DNA topoisomerase (ATP-hydrolyzing) medium chain homology <T4

Query Match 100.0%; Score 49; DB 2; Length 1526;
Best Local Similarity 100.0%; Pred. No. 0.34;
Matches 9; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
QY 1 FLYDDNQRV 9
|||||
DB 826 FLYDDNQRV 834

RESULT 4

A44406
DNA topoisomerase (ATP-hydrolyzing) (EC 5.99.1.3) - Chinese hamster
N;Alternate names: DNA-gyrase; type II DNA topoisomerase
C;Species: Cricetulus griseus (Chinese hamster)
C;Date: 31-Dec-1993 #sequence_revision 31-Dec-1993 #text_change 09-Jul-2004
C;Accession: A44406
R;Chan, V.T.; Ng, S.W.; Eder, J.P.; Schnipper, L.B.
J. Biol. Chem. 268, 2160-2165, 1993
A;Title: Molecular cloning and identification of a point mutation in the topoisomerase I
A;Reference number: A44406; MUID:93131977; PMID:8380592
A;Accession: A44406
A;Molecule type: nucleic acid
A;Residues: 1-1526 <CHA>
A;Cross-references: UNIPROT:P41515; GB:L04607; NID:G191217; PIDN:AAA37023.1; PID:G191218
A;Experimental source: ovary
A;Note: sequence extracted from NCBI backbone (NCBIP:123211)
C;Superfamily: eukaryotic type II DNA topoisomerase; phase T4 DNA topoisomerase (ATP-hy
C;Keywords: ATP; DNA binding; DNA replication; heterotrimer; isomerase

Query Match 100.0%; Score 49; DB 2; Length 1526;
Best Local Similarity 100.0%; Pred. No. 0.34;
Matches 9; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
QY 1 FLYDDNQRV 9
|||||
DB 827 FLYDDNQRV 835

RESULT 5

JS0703
DNA topoisomerase (ATP-hydrolyzing) (EC 5.99.1.3) II - mouse
C;Species: Mus musculus (house mouse)
C;Date: 16-Sep-1992 #sequence_revision 16-Sep-1992 #text_change 09-Jul-2004

C;Accession: JS0703; S35483
R;Adachi, N.; Miyaike, M.; Ikeda, H.; Kikuchi, A.
submitted to JIPID, July 1992
A;Reference number: JS0703
A;Accession: JS0703
A;Status: translation not shown
A;Molecule type: mRNA
A;Residues: 1-1528 <ADA>
A;Cross-references: UNIPROT:O01320; DDBJ:D12513; NID:G220615; PIDN:BAA02076.1; PID:G22

R;Adachi, N.; Miyaike, M.; Ikeda, H.; Kikuchi, A.
Nucleic Acids Res. 20, 5297-5303, 1992
A;Title: Characterization of cDNA encoding the mouse DNA topoisomerase II that can cor
A;Reference number: S35483; MUID:93065194; PMID:1331984
A;Accession: S35483
A;Status: preliminary
A;Molecule type: mRNA
A;Residues: 1-1528 <ADA2>
A;Cross-references: EMBL:D12513; NID:G220615; PIDN:BAA02076.1; PID:G220616

C;Superfamily: eukaryotic type II DNA topoisomerase; phase T4 DNA topoisomerase (ATP-h
C;Keywords: ATP; DNA binding; isomerase; leucine zipper; nucleus
F;994-1015/Region: leucine zipper motif
F;804/Active site: Tyr #status predicted
Query Match 100.0%; Score 49; DB 2; Length 1528;
Best Local Similarity 100.0%; Pred. No. 0.34;
Matches 9; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
QY 1 FLYDDNQRV 9
|||||
DB 827 FLYDDNQRV 835

RESULT 6

A40493
DNA topoisomerase (ATP-hydrolyzing) (EC 5.99.1.3) alpha - human
C;Species: Homo sapiens (man)
C;Date: 07-Feb-1992 #sequence_revision 03-Apr-1992 #text_change 19-Dec-1998
C;Accession: A40493; A41278
R;Tsai-Pflugfelder, M.; Liu, L.F.; Liu, A.A.; Tewey, K.M.; Whang-Peng, J.; Knutsen, T.
Proc. Natl. Acad. Sci. U.S.A. 85, 7177-7181, 1988
A;Title: Cloning and sequencing of cDNA encoding human DNA topoisomerase II and local
A;Reference number: A40493; MUID:89017161; PMID:2845399
A;Accession: A40493
A;Molecule type: mRNA
A;Residues: 1-1530 <TSA>
A;Cross-references: GB:J04088
R;Bug, B.Y.; Danks, M.K.; Beck, W.T.; Suttle, D.P.
Proc. Natl. Acad. Sci. U.S.A. 88, 7654-7658, 1991
A;Title: Expression of a mutant DNA topoisomerase II in CCRF-CEM human leukemic cells;
A;Reference number: A41278; MUID:91352047; PMID:1652758
A;Accession: A41278
A;Status: not compared with conceptual translation
A;Molecule type: mRNA
A;Residues: 442-521 <BUG>
A;Note: a mutant with residue 449-Arg replaced by Gln was resistant to teniposide

C;Genetics:
A;Gene: GDB:TOP2A; TOP2
A;Cross-references: GDB:118884; OMIM:126430
A;Map position: 17q21-17q22
C;Superfamily: eukaryotic type II DNA topoisomerase; phase T4 DNA topoisomerase (ATP-h
C;Keywords: ATP; DNA binding; isomerase; nucleus
Query Match 100.0%; Score 49; DB 2; Length 1530;
Best Local Similarity 100.0%; Pred. No. 0.34;
Matches 9; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
QY 1 FLYDDNQRV 9
|||||
DB 827 FLYDDNQRV 835

RESULT 7

S59969

Exhibit B Page 1 of 2

GenCore version 5.1.6
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OM protein - protein search, using sw model

Run on: December 29, 2004, 16:22:15 ; Search time 38 Seconds
(without alignments)
15.707 Million cell updates/sec

Title: US-10-006-177-4

Perfect score: 49

Sequence: 1 FLYDDNQRV 9

Scoring table: BLOSUM62

Gapop 10.0 , Gapext 0.5

Searched: 478139 seqs, 66318000 residues

Total number of hits satisfying chosen parameters: 478139

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

Database :

Issued Patents AA.*
1: /cgn2_6/ptodata/1/iaa/5A COMB.pep.*
2: /cgn2_6/ptodata/1/iaa/5B COMB.pep.*
3: /cgn2_6/ptodata/1/iaa/6A COMB.pep.*
4: /cgn2_6/ptodata/1/iaa/6B COMB.pep.*
5: /cgn2_6/ptodata/1/iaa/PTCUS COMB.pep.*
6: /cgn2_6/ptodata/1/iaa/backfiles.pep.*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	ID	Description
1	49	100.0	1531	US-09-976-594-203	Sequence 203, Appl
2	43	87.8	142	US-08-470-179-60	Sequence 30, Appl
3	37	75.5	324	US-09-270-767-43224	Sequence 43224, A
4	36	73.5	189	US-09-328-352-6722	Sequence 6722, Ap
5	36	73.5	1665	US-09-543-681A-4476	Sequence 4476, Ap
6	35	71.4	233	US-09-543-681A-4354	Sequence 4354, Ap
7	35	71.4	855	US-09-543-681A-7287	Sequence 7287, Ap
8	34	69.4	235	US-08-580-545B-10	Sequence 10, Appl
9	34	69.4	235	US-09-262-653A-10	Sequence 10, Appl
10	34	69.4	457	US-09-248-796A-23295	Sequence 23295, A
11	33	67.3	64	US-08-765-179B-19	Sequence 19, Appl
12	33	67.3	108	US-08-259-372A-10	Sequence 10, Appl
13	33	67.3	108	US-08-468-671-10	Sequence 10, Appl
14	33	67.3	108	US-09-025-769B-20	Sequence 20, Appl
15	33	67.3	108	US-09-490-070A-20	Sequence 20, Appl
16	33	67.3	108	US-09-490-153-20	Sequence 20, Appl
17	33	67.3	109	US-09-157-370-5	Sequence 5, Appl
18	33	67.3	113	US-09-377-285B-65	Sequence 65, Appl
19	33	67.3	130	US-09-270-767-61055	Sequence 61055, A
20	33	67.3	522	US-08-894-818B-3	Sequence 3, Appl
21	33	67.3	522	US-09-445-472-4	Sequence 4, Appl
22	33	67.3	522	US-10-090-624-4	Sequence 4, Appl
23	33	67.3	554	US-08-894-818B-35	Sequence 35, Appl
24	33	67.3	654	US-09-445-472-16	Sequence 16, Appl
25	33	67.3	654	US-10-090-624-16	Sequence 16, Appl
26	33	67.3	684	US-09-823-240A-9	Sequence 9, Appl
27	33	67.3	715	US-09-252-991A-27965	Sequence 27965, A

28 67.3 102 1 US-08-701-846-2 Sequence 2, Appl
29 65.3 109 3 US-09-025-769B-32 Sequence 32, Appl
30 65.3 109 3 US-09-025-769B-51 Sequence 51, Appl
31 65.3 109 4 US-09-490-070A-32 Sequence 32, Appl
32 65.3 109 4 US-09-490-070A-51 Sequence 51, Appl
33 65.3 109 4 US-09-490-153-32 Sequence 32, Appl
34 65.3 109 4 US-09-490-153-51 Sequence 51, Appl
35 65.3 234 4 US-09-372-425A-4 Sequence 4, Appl
36 65.3 242 3 US-08-884-569A-5 Sequence 5, Appl
37 65.3 286 4 US-09-489-039A-10682 Sequence 10682, A
38 65.3 304 4 US-09-248-796A-16060 Sequence 16060, A
39 65.3 359 4 US-09-248-796A-14544 Sequence 14544, A
40 65.3 528 4 US-09-248-796A-17909 Sequence 17909, A
41 65.3 1584 3 US-09-251-645-6 Sequence 6, Appl
42 31.5 64.3 254 4 US-09-266-965-123 Sequence 123, App
43 63.3 99 4 US-09-107-532A-5802 Sequence 5802, Ap
44 63.3 112 2 US-08-665-202-39 Sequence 39, Appl
45 63.3 112 4 US-09-315-574-39 Sequence 39, Appl

ALIGNMENTS

RESULT 1

US-09-976-594-203
; Sequence 203, Application US/09976594
; Patent No. 6673549
; GENERAL INFORMATION:
; APPLICANT: Furness, Michael
; APPLICANT: Buchsinger, Jenny
; TITLE OF INVENTION: GENES EXPRESSED IN C3A LIVER CELL CULTURES TREATED WITH STEROIDS
; FILE REFERENCE: PA-0041 US
; CURRENT APPLICATION NUMBER: US/09/976,594
; CURRENT FILING DATE: 2001-10-12
; PRIOR APPLICATION NUMBER: 60/240,409
; PRIOR FILING DATE: 2000-10-12
; NUMBER OF SEQ ID NOS: 1143
; SOFTWARE: PERL Program
; SEQ ID NO 203
; LENGTH: 1531
; TYPE: PRT
; ORGANISM: Homo sapiens
; FEATURE:
; NAME/KEY: misc_feature
; OTHER INFORMATION: Incyte ID No. 6673549 1867417CD1
US-09-976-594-203

Query Match 100.0%; Score 49; DB 4; Length 1531;
Best Local Similarity 100.0%; Pred. No. 1;
Matches 9; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 FLYDDNQRV 9
Db 828 FLYDDNQRV 836

RESULT 2

US-08-470-179-30
; Sequence 30, Application US/08470179
; Patent No. 5645994
; GENERAL INFORMATION:
; APPLICANT: Huang Ph.D, Wai Mun
; TITLE OF INVENTION: Method and Compositions for
; TITLE OF INVENTION: Identification of Species in a Sample
; NUMBER OF SEQUENCES: 207
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: Trask, Britt and Rossa
; STREET: P. O. Box 2550
; CITY: Salt Lake City
; STATE: Utah
; COUNTRY: USA
; ZIP: 84110
; COMPUTER READABLE FORM:

MEDIUM TYPE: Floppy disk
COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: Patent In Release #1.0, Version #1.30
CURRENT APPLICATION DATA:
APPLICATION NUMBER: US/08/470,179
FILING DATE:
CLASSIFICATION: 435
ATTORNEY/AGENT INFORMATION:
NAME: Swelgert Ph.D, Susan E.
REGISTRATION NUMBER: 36,289
REFERENCE/DOCKET NUMBER: 2601
TELECOMMUNICATION INFORMATION:
TELEPHONE: 801-532-1922
TELEFAX: 801-531-9168
INFORMATION FOR SEQ ID NO: 30:
SEQUENCE CHARACTERISTICS:
LENGTH: 142 amino acids
TYPE: amino acid
STRANDEDNESS:
TOPOLOGY: not relevant
MOLECULE TYPE: protein
HYPOTHETICAL: NO
ANTI-SENSE: NO
FRAGMENT TYPE: internal
ORIGINAL SOURCE:
ORGANISM: Homo sapiens sapiens
US-08-470-179-30

Query Match 87.8%; Score 43; DB 1; Length 142;
Best Local Similarity 100.0%; Pred. No. 1.1;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 2 FLYDDNQRV 9
DB 110 FLYDDNQRV 117

RESULT 3
US-09-270-767-43224
Sequence 43224, Application US/09270767
Patent No. 6703491
GENERAL INFORMATION:
APPLICANT: Homburger et al.
TITLE OF INVENTION: Nucleic acids and proteins of Drosophila melanogaster
FILE REFERENCE: File Reference: 7326-094
CURRENT APPLICATION NUMBER: US/09/270,767
CURRENT FILING DATE: 1999-03-17
NUMBER OF SEQ ID NOS: 62517
SOFTWARE: Patent In Ver. 2.0
SEQ ID NO 43224
LENGTH: 324
TYPE: PRT
ORGANISM: Drosophila melanogaster
US-09-270-767-43224

Query Match 75.5%; Score 37; DB 4; Length 324;
Best Local Similarity 77.8%; Pred. No. 33;
Matches 7; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

QY 1 FLYDDNQRV 9
DB 59 YLTDNQRV 67

RESULT 4
US-09-328-352-6722
Sequence 6722, Application US/09328352
Patent No. 6562958
GENERAL INFORMATION:
APPLICANT: Gary L. Breton et al.
TITLE OF INVENTION: NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO ACINETOBACTER
TITLE OF INVENTION: BAUMANNII FOR DIAGNOSTICS AND THERAPEUTICS

FILE REFERENCE: GTC95-03PA
CURRENT APPLICATION NUMBER: US/09/328,352
CURRENT FILING DATE: 1999-06-04
NUMBER OF SEQ ID NOS: 8252
SEQ ID NO 6722
LENGTH: 189
TYPE: PRT
ORGANISM: Acinetobacter baumannii
US-09-328-352-6722

Query Match 73.5%; Score 36; DB 4; Length 189;
Best Local Similarity 85.7%; Pred. No. 29;
Matches 6; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

QY 3 YDDNQRV 9
DB 108 YDDNQRV 114

RESULT 5
US-09-543-681A-4476
Sequence 4476, Application US/09543681A
Patent No. 6605709
GENERAL INFORMATION:
APPLICANT: GARY BRETON
TITLE OF INVENTION: NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO PROTEUS MIRAI
FILE REFERENCE: 2709.1002-001
CURRENT APPLICATION NUMBER: US/09/543,681A
CURRENT FILING DATE: 2000-04-05
PRIOR APPLICATION NUMBER: US 60/128,706
PRIOR FILING DATE: 1999-04-09
NUMBER OF SEQ ID NOS: 8344
SEQ ID NO 4476
LENGTH: 1665
TYPE: PRT
ORGANISM: Proteus mirabilis
US-09-543-681A-4476

Query Match 73.5%; Score 36; DB 4; Length 1665;
Best Local Similarity 66.7%; Pred. No. 2.7e+02;
Matches 6; Conservative 2; Mismatches 1; Indels 0; Gaps 0;

QY 1 FLYDDNQRV 9
DB 723 FYDDYQRM 731

RESULT 6
US-09-543-681A-4354
Sequence 4354, Application US/09543681A
Patent No. 6605709
GENERAL INFORMATION:
APPLICANT: GARY BRETON
TITLE OF INVENTION: NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO PROTEUS MIRAB
FILE REFERENCE: 2709.1002-001
CURRENT APPLICATION NUMBER: US/09/543,681A
CURRENT FILING DATE: 2000-04-05
PRIOR APPLICATION NUMBER: US 60/128,706
PRIOR FILING DATE: 1999-04-09
NUMBER OF SEQ ID NOS: 8344
SEQ ID NO 4354
LENGTH: 233
TYPE: PRT
ORGANISM: Proteus mirabilis
US-09-543-681A-4354

Query Match 71.4%; Score 35; DB 4; Length 233;
Best Local Similarity 75.0%; Pred. No. 54;
Matches 6; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

QY 1 FLYDDNQRV 8